

Translation

PATENT COOPERATION TREATY

PCT/FR2003/001873



PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 344915D20427	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/FR2003/001873	International filing date (<i>day/month/year</i>) 18 juin 2003 (18.06.2003)	Priority date (<i>day/month/year</i>) 18 juin 2002 (18.06.2002)
International Patent Classification (IPC) or national classification and IPC C07D 401/12, A61K 31/506, A61P 25/00		
Applicant PIERRE FABRE MEDICAMENT		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☒ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 13 janvier 2004 (13.01.2004)	Date of completion of this report 23 September 2004 (23.09.2004)
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/FR2003/001873

I. Basis of the report

1. With regard to the elements of the international application:*

- ☒ the international application as originally filed
- ☒ the description:
pages 1-22, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____
- ☒ the claims:
pages 1-8, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages _____, filed with the letter of _____
- ☐ the drawings:
pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____
- ☐ the sequence listing part of the description:
pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

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IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☐ restricted the claims.
- ☐ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
- ☒ not complied with for the following reasons:

See supplemental sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☒ all parts.
- ☐ the parts relating to claims Nos. _____

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: IV.

The present International Searching Authority considers that the following two subjects are not linked by a technical relationship under the terms of PCT Rule 13.2 and that, as a result, the application does not fulfil the requirement of unity of invention set forth in PCT Rule 13.1. The reasons are as follows:

Document D1 is cited in this report: D1: WO 98/22459.

In said document, example I-66 describes a compound having Formula I, wherein $X=Y=CH$, $A=Me$, $B=F$, $D=Cl$ and $E=F$. This compound is used as a 5-HT_{1A} agonist. This compound has been excluded from claim 1 of the present application.

The only feature in the application that could constitute a special technical feature is Formula I. This feature is not novel (D1). Since it has not been possible to identify other features in the present application that could constitute special technical features, the present application lacks unity. The two subjects are:

1. Compounds having general formula (I), wherein $X=Y=CH$, and the compositions and uses thereof.
2. Compounds having general formula (I), wherein $X=Y=N, CH$, except those compounds in which $X=Y=CH$, and the compositions and uses thereof.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/FR 03/01873

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-8	YES .
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-8	NO
Industrial applicability (IA)	Claims	1-8	YES
	Claims		NO

2. Citations and explanations

SUBJECT 1

The present application does not fulfil the requirements set forth in PCT Article 33(3) because the subject matter of claims 1-8 does not involve an inventive step.

Reference is made to the following document:

D1: WO 98/22459 A (KOEK WOUTER; PF MEDICAMENT (FR); BONNAUD BERNARD (FR); VACHER BERN) 28 May 1998 (1998-05-28).

The closest subject matter is described in document D1 (page 79, the table). Example I-66 describes a compound that falls within the scope of claim 1 of the present application. This compound has been excluded from claim 1 of the present application. Said compound has the same activity as the compounds of the present application.

Compound I-66 was not tested in document D1 and was only tested in the present application. Apparently, the activity of said compound is inferior to that of the compounds in example 9 (75% versus 100% stimulation, see the table on page 21).

The compounds tested in document D1 were compounds I-62, I-65 and I-55. Said compounds also have high 5-HT_{1A}/D2 selectivity.

The present application relates, in particular, to compounds having general formula (I), wherein B and E each represent a fluorine atom and D represents a chlorine atom. Compounds I-62 and I-55 also have these features but, unlike compound I-66, have not been tested with regard to stimulation in the present application.

In the present application, the problem addressed by the applicant was that of providing compounds with enhanced specific activity with respect to 5-HT_{1A}. It is not clear that all of the compounds claimed in claim 1 have superior activity to the compounds of D1. For this reason, claims 1-8 do not involve an inventive step.

Moreover, it appears that the claim does not include all of the essential features. It was necessary to include a proviso but said proviso is not a positive feature. It is not clear why the activity of compound I-66 is inferior to that of the compounds claimed in claim 1.

SUBJECT 2

Claims 1 and 2 describe compounds having general formula (I), wherein

- (a) X or Y is CH and the other is N and they cannot be the same; and
- (b) X=Y=N.

Feature (b) of subject 2 is not supported by the description. There are no examples of feature (b) in the

present application. It follows that feature (b) of subject 2 (claims 1, 2, 4-8) of the present application does not fulfil the requirements of PCT Article 6.

Feature (a) of subject 2 involves an inventive step. In the present application, the problem addressed by the applicant was that of providing alternative compounds having specific activity with respect to 5-HT_{1A}. The closest prior art is document D1, which describes compounds in which the piperidin-4-yl group has been substituted with a methyl pyridine group. The difference between D1 and the present application is that the compounds of the present application have a pyrimidine group, whereas the compounds of document D1 have a pyridine group. It would not have been obvious for a person skilled in the art to replace a pyridine with a pyrimidine and, as a result, feature (a) of subject 2 involves an inventive step.